PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Fritz Sieber, et al.
Serial No.:	10/701,870
Filed:	November 5, 2003
For:	METHOD OF MAKING, AND THE USE OF CYTOTOXIC AGENTS CONTAINING ELEMENTAL SELENIUM
Group Art Unit:	1653
Examiner:	Tsay, Marsha
Ref. No.;	650053.91649

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner For Patents
Alexandria, VA 22313-1450

Dear Sir:

I, Fritz Sieber, on oath say and declare that:

1. I am the same Fritz Sieber who is one of the named inventors of the above-identified patent application. I am currently employed as a Professor of Pediatrics and Medicine at the Medical College of Wisconsin, a position that I have held since 1985 (Associate Professor) and 1990 (Full Professor), respectively. I obtained my Ph.D (Dr sc nat ETH) degree in Biology in 1976 from the Swiss Federal Institute of Technology in Zurich. I have worked as a research scientist specializing in the general area of cancer research for 30 years. For the last 18 years, my research has focused on selenomerocyanine photosensitizers and their cytotoxic photoproducts (elemental selenium). I have published extensively in the area. A copy of my Curriculum Vitae is attached as Exhibit A.

2. I have reviewed the Office Action issued in this matter by the U.S. Patent and Trademark Office on April 28, 2006. I understand that claims 2, 4-6, 8, and 9 are rejected as being anticipated by Lou et al. (Clinical Chemistry 39:619-624, 1993) and claims 7 and 10-12 are rejected as being obvious over Lou et al. in view of Zhang et al. (BioFactors 15:27-38, 2001), in part because of the Examiner's concern that the inventors have not provided evidence on the size of the Se(0) particles produced and tested by the inventors. This Declaration is submitted to

provide evidence that the Se(0) particles produced and tested by the inventors have diameters of about 0.4 nm to about 1 nm.

3. Currently, it is difficult to measure Se(0) particles of 1.8 nm or smaller directly because the resolution of standard electron microscopy combined with energy dispersive X-ray analysis (EDX) is about 1.8 nm. Therefore, unlike Zhang et al. who were able to directly measure the Se(0) particles of 20-60 nm they produced by electron microscopy, we estimated the size of the Se(0) particles we produced by indirect evidence. Nevertheless, as provided below, the conclusion is scientifically sound.

4. We collaborated with Dr. William D. James (Texas A&M University) and Dr. JoAn Hudson (Clemson University) who conducted chemical and electron microscopy (resolution: 1.8 nm) analyses on our Se composition. The chemical analysis performed by inductively coupled plasma mass spectroscopy (ICP-MS) shows that our composition contains selenium in the predicted amounts. It also shows that the selenium is not removed by dialysis (molecular weight cutoff: 7 kDa), indicating that the selenium is firmly associated with the macromolecular fraction. The electron microscopic analysis, which had a resolution of 1.8 nm, failed to reveal discrete particles of selenium, indicating that the selenium moiety in our Se(0)-selenium conjugates had a diameter of less than 1.8 nm.

5. We determined from dose-response experiments that Se(0) particles bound to the mercaptalbumin molecules in our Se composition have 6 to 8 Se atoms (see sections 6-9 below for details). Se6 and Se 8 rings (i.e., Se(0) particles with 6 and 8 Se atoms, respectively) are well known stable structures of Se(0) in the art (see e.g., Ralph A. Zingaro and W. Charles Cooper (Eds): Selenium, The Van Nostrand Reinhold Company, New York, 1974; and Takahashi T et al., Physical Review B (Condensed Matter) 28:4893-4895, 1983). By molecular modeling in Chem3D Pro (CambridgeSoft, Cambridge, MA), a software program widely used in the art and proved to be effective with many chemicals for 3-dimensional modeling, we found in consistency with the above literature as well as the chemical and electron microscopy (resolution: 1.8 nm) analyses that Se6 or Se8 forms a ring structure that resembles a slightly distorted doughnut with the largest diameter being about 1 nm and the smallest diameter being about 0.4 nm. Based on the above evidence, we concluded that the Se(0) particles we produced are from about 0.4 nm to about 1 nm.

6. The dose-response experiments to which section 5 refers are described in detail below. At my discretion and under my supervision, members of my laboratory conducted the following experiments:

7. Experiment A: Equal concentrations (26 μM) of a selenomerocyanine dye were photobleached in tissue culture medium that contained equal concentrations (26 μM) of either native bovine serum albumin or carboxymethylated albumin obtained from a commercial source (Sigma, St Louis, MO). The photobleached solutions were subsequently assayed for cytotoxic activity by *in vitro* clonal assay using L1210 leukemia cells as targets. Only dye that was photobleached in the presence of native albumin generated cytotoxic activity. Dye that was photobleached in the presence of carboxymethylated albumin did not generate cytotoxic activity. The significance of this finding is as follows. Virtually all known albumins (including human and bovine albumin) contain 35 cysteine residues. Thirty-four of the 35 cysteines form disulfide bonds. Only one cysteine (CySH-34) is present as a free thiol. In carboxymethylated albumin, CySH-34 is specifically blocked. Failure to generate cytotoxic activity in the presence of carboxymethylated albumin thus indicates that the free thiol at CySH-34 is essential for the formation of cytotoxic Se(0)-protein conjugates. The fact that blockage of a single site completely prevents the formation of cytotoxic activity also argues that multiple atoms of selenium interact as a single entity (e.g., cyclic molecule of 6-8 Se atoms) with a single site (CySH-34) rather than as individual Se atoms with a multitude of sites.

8. Experiment B: To corroborate the critical role of CySH-34 in the formation of cytotoxic Se(0)-protein conjugates, we co-incubated target cells with cytotoxic conjugates and a low dose of the anti-cancer drug cisplatin (CDDP). Cisplatin is known to react covalently with CySH-34. As Fig. 27 of this application shows, cisplatin antagonized the cytotoxic activity of Se(0)-protein conjugates, most likely by displacing Se(0) from CySH-34. For experimental details please see legend to Fig. 27.

9. Experiment C: To determine how many Se atoms combined with albumin, graded concentrations of a selone dye were mixed with a fixed concentration of albumin, photobleached, and assayed for cytotoxic activity as described in Fig. 7 of the application. As Fig. 7 shows, a dye:protein molar ratio of about 4.5:1 was saturating. Taking into consideration the crucial role of CySH-34 in the formation of cytotoxic activity and the fact that in commercial preparations of serum albumin such as the one used for this experiment, the actual free thiol concentration is

only about 0.7 M/M, an apparent saturating dose of 4.5:1 suggests that mercaptalbumin binds about 6-8 Se atoms (most likely in the form of Se_6 and/or Se_8) whereas the non-mercaptalbumin molecules bind none.

10. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated this 19th day of September, 2006.

Fritz Sieber

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CURRICULUM VITAE

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Education:

1966 Matura, Kantonsschule Zug

1971 Dipl Natw ETH (MS), Swiss Federal Institute of Technology, Zürich. Thesis on purification and characterization of octanol dehydrogenase and elucidation of its role in the development of Drosophila. Adviser: Heinrich Urspung, PhD

1976 Dr sc nat ETH (PhD), Swiss Federal Institute of Technology, Zürich. Thesis on the purification and characterization of human erythropoietin and its interactions with erythroid progenitor cells. Adviser: Heinrich Ursprung, PhD

Postgraduate Training and Fellowship Appointments:

1976-1979 Swiss National Science Foundation Fellow, Department of Biology, The Johns Hopkins University, Baltimore. Research on cell-cell recognition and adhesion. Adviser: Saul Roseman, PhD

Faculty Appointments:

1979-1985 Assistant Professor of Medicine, The Johns Hopkins University School of Medicine, Baltimore

1980-1985 Assistant Professor of Oncology, The Johns Hopkins University School of Medicine, Baltimore

1985-1990 Associate Professor of Pediatrics (Hematology/Oncology), Medical College of Wisconsin, Milwaukee

1986- Joint appointments in Department of Cell Biology, Neurobiology & Anatomy, Department of Microbiology & Molecular Genetics, and Biophysics Program

1990-1992 Professor of Pediatrics (Hematology/Oncology), Medical College of Wisconsin, Milwaukee

1992- Professor of Pediatrics & Medicine (Cancer and Blood Diseases) with Tenure, Medical College of Wisconsin, Milwaukee

Awards and Honors:

1966	Willy Beusch-Prize, Zug
1976	Swiss National Science Foundation Fellowship
1977	Swiss National Science Foundation Fellowship
1978	Scholarship for Advanced Young Scientists from Swiss National Science Foundation
1980	Hubert E and Anne E Rogers Award
1984	Leukemia Society of America Scholar
1987	Frederick Stohlman Memorial Award of the Leukemia Society of America

Membership in Professional Societies:

1974-	Union of Swiss Societies of Experimental Biology
1975-	International Society for Differentiation
1978-	American Association for the Advancement of Science
1978-	American Society for Cell Biology
1979-	International Society for Experimental Hematology 1982: Member, Organizing Committee, Annual Meeting 1982: Session Chairman 1991: Co-organizer and co-chairman, Satellite Symposium on Photobiology and Photomedicine
1974-	New York Academy of Sciences
1980-	Society of General Physiologist
1980-	International Society of Developmental Biologists
1981-	American Society of Hematology 1983: Session Chairman
1982-	American Federation for Clinical Research
1982-	Society for Analytical Cytology
1983-	International Association for Comparative Research on Leukemia and Related Diseases
1985-	American Society for Photobiology 1994: Session Chairman 1997: Symposium Organizer
1986-	Pediatric Oncology Group
1987-	American Association for Cancer Research
1990-	International Photodynamic Association 2006: Scientific Committee, 11th World Congress 2007: Session Chair, 11th World Congress
1993-	International Society for Hematotherapy & Graft Engineering
1997-	American Chemical Society

Editorial Boards:

1987-1992	Associate editor, Cancer Therapy and Control
1992-2002	Editorial board, Cancer Research, Therapy & Control
1997-2002	Section editor, Cancer Research, Therapy & Control
2006-	Editorial board, Current Chemical Biology
1985-	Ad hoc reviewer for Blood, Cancer Research, Experimental Hematology, Bone Marrow Transplantation, Photochemistry and Photobiology, Transfusion, Proceedings of the National Academy of Sciences USA, British Journal of Cancer, Transplantation, Leukemia Research, Biochimica et Biophysica Acta, Journal of Photochemistry & Photobiology, Laboratory Investigation, International Journal of Radiation Biology, Archives of Biochemistry and Biophysics, Clinical Cancer Research, International Journal of Cancer, Cancer Detection and Prevention, Anatomical Record, Biology of Blood and Marrow Transplantation, Free Radical Biology and Medicine, Molecular Cancer Therapeutics, Acta Pharmacologica Sinica.

National Advisory Committees and Activities:

1985-1988	Ad hoc member, Experimental Therapeutics Study Section, NIH
1985-1986	Ad hoc reviewer, Veterans Administration
1987	Member, Organizing Committee, Leukemia Society of America 4th Annual Meeting
1990	Ad hoc reviewer, American Red Cross
1992	Ad hoc reviewer, Alberta Heritage Foundation for Medical Research
1994	Member, Special Emphasis Review Panel, National Heart, Lung, and Blood Institute
1994	Organizer, Symposium "Advances in Photodynamic Therapy and the Fluorescence Detection of Small Tumors"
1995	Experimental Therapeutics-1 Study Section, NIH
1996	Ad hoc reviewer, Veterans Administration
1997	Ad hoc reviewer, Medical Research Council of Canada
1998	Ad hoc reviewer, Hematology Study Section, NIH
2000	Member, Special Emphasis Review Panel, Experimental Therapeutics-2 Study Section, NIH

Community Advisory Committees and/or Activities:

Board member and chairman Special Gifts Committee, American Cancer Society-Milwaukee

Member, Peer Review Committee, American Heart Association-Wisconsin Affiliate

Invited Lectures, Workshops and Site Visits:

Invited Lectures

2005

01/22 Photonics West, BiOS 2005, Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy. San Jose, CA.

2004

02/24 Inaugural Plenary Lecture, 9th International Conference on the Chemistry of Selenium and Tellurium (ICCST-9), Bombay, India.

2003

08/12 National Cancer Institute, Rockville, MD

1999

07/15 Immunotech SA, Marseille, France

1998

02/12 University of Wisconsin-Madison, School of Engineering, Wisconsin Center for Space Automation and Robotics, Madison, WI.

06/22 Theratechnologies, Inc. and McGill University, Montreal, Canada

1997

07/05 Workshop "Photopheresis: Paradigms and Mechanisms"
25th Annual Meeting of the American Society for Photobiology,
St. Louis, MO

07/09 Symposium "New Developments in Extracorporeal Photochemotherapy"
25th Annual Meeting of the American Society for Photobiology,
St. Louis, MO

10/24 University of Wisconsin-Madison, School of Pharmacy, Madison, WI.

1996

01/11 Space Technology and Applications International Forum, Albuquerque, NM

1995

05/06 Fourth Great Lakes PDT Conference, Detroit, MI

1994

02/10 The Temple University Cancer Center, Philadelphia, PA.

09/19 Symposium "Advances in Photodynamic Therapy and the Fluorescence Detection of Small Tumors", Children' Hospital of Wisconsin, Milwaukee, WI

1993

06/29 Symposium on Photochemical Blood Sterilization, 21st Annual Meeting of the American Society for Photobiology, Chicago, IL
09/17 4th International on Bone Marrow Purging and Processing, Orlando, FL

1992

05/27 Symposium on DNA Cleavage and Viral Inactivation, American Chemical Society Regional Meeting, Cincinnati, OH
06/24 Symposium on the Sterilization of Blood by Light, 20th Annual Meeting of the American Society for Photobiology, Marco Island, FL
09/10 11th International Congress on Photobiology, Kyoto, Japan

1991

06/24 Symposium on the Photoinactivation of Viruses and Cells for Medical Applications, 19th Annual Meeting of the American Society for Photobiology, San Antonio, TX
07/27 Satellite Symposium on Photobiology and Photomedicine, 20th Annual Meeting of the International Society for Experimental Hematology, Parma, Italy
09/03 4th Congress of the European Society for Photobiology, Amsterdam, The Netherlands
11/02 6th Annual Meeting of the Clinical Immunology Society, Arlington, VA

1990

01/20 SPIE Think Tank on the Future of Photodynamic Therapy, San Diego, CA
03/26 Therapeutic Immunology Inc, Minneapolis, MN
06/20 Annual Meeting, American Society for Photobiology, Vancouver, BC
06/21 Photodynamic Therapy Workshop, University of British Columbia, Vancouver, BC
10/04 The James Graham Brown Cancer Center, University of Louisville, Louisville, KY

1989

01/05 Quadra Logic Technologies and University of British Columbia, Vancouver, BC, Canada
03/20 Wayne State University, Detroit, MI
07/20 18th Annual Meeting, International Society for Experimental Hematology, Paris, France
12/05 31st Annual Meeting, American Society of Hematology, Atlanta, GA

1988

04/06 Eastman Pharmaceuticals, Great Valley, PA
06/15 Leukemia Society of America-Wisconsin
07/20 Sterling Research Group, Malvern, PA
08/20 4th International Symposium on Autologous Bone Marrow Transplantation, Houston, TX
09/07 Advances in Photochemotherapy, Boston, MA
10/27 Sterling Research Group, Malvern, PA

1987

02/13 First International Workshop on Bone Marrow Purging, Orlando, FL
02/17 Photodynamic Therapy Conference, Marina del Rey, CA
03/05 The New York Blood Center, New York, NY
03/19 Third National Leukemia Society of America Symposium, San Diego, CA
10/09 St. Jude Children's Research Hospital, Memphis, TN
10/29 Conference on New Directions in Photodynamic Therapy, Cambridge, MA

1986

01/14 Memorial Sloan-Kettering Cancer Center, New York, NY
02/13 Developmental and Clinical Investigation Program, Sloan-Kettering Institute, New York, NY
07/07 Eastman-Kodak Company, Rochester, NY
10/11 Wisconsin Dermatological Society

1985

02/12 Upstate Medical Center, Syracuse, NY
03/06 The Upjohn Company, Kalamazoo, MI
07/09 Autologous Bone Marrow Transplant Meeting, Parma, Italy
11/07 Second International Symposium on Detection and Treatment of Minimal Residual Disease in Leukemia, Rotterdam, The Netherlands

Site Visits

1994

03/22 National Cancer Institute, program project grant (Case Western Reserve University, Cleveland, OH)

1993

02/22-02/24 National Cancer Institute, program project grant (Case Western Reserve University, Cleveland, OH)

1990

03/07 National Cancer Institute, program project grant (Case Western Reserve University)

1989

06/05-06/07 National Cancer Institute, program project grant (University of Toledo, Medical College of Ohio, Wayne State University, University of Michigan Ann Arbor).

BIBLIOGRAPHY

ORIGINAL PAPERS

1. Sieber F, Fox DJ and Ursprung H: Properties of octanoldehydrogenase from Drosophila. FEBS Letters 26:274-276, 1972.

2. Madhavan K, Conscience-Egli M, Sieber F and Ursprung H: Farnesol metabolism in Drosophila melanogaster: ontogeny and tissue distribution of octanoldehydrogenase and aldehyde oxidase. J Insect Physiol 19:235-241, 1973.

3. Iscove NN, Sieber F and Winterhalter KH: Erythroid colony formation in cultures of mouse and human bone marrow: analysis of the requirement for erythropoietin by gel filtration and affinity chromatography on agarose-concanavalin-A. J Cell Physiol 83:309-320, 1974.

4. Iscove NN and Sieber F: Erythroid progenitors in mouse bone marrow detected by macroscopic colony formation in culture. Exp Hematol 3:32-43, 1975.

5. Sieber F: Chromatography of human urinary erythropoietin and granulocyte colony stimulating factor on insolubilized phytohaemagglutinin. Biochim Biophys Acta 496:146-154, 1977.

6. Sieber-Blum M, Sieber F and Yamada KM: Cellular fibronectin promotes development of quail neural crest cells in vitro. Exp Cell Res 133:285-295, 1981.

7. Sieber F, Meagher RC and Spivak JL: Differential sensitivity of mouse hematopoietic stem cells to merocyanine 540. Differentiation 19:65-67, 1981.

8. Sieber F and Roseman S: Quantitative analysis of intercellular adhesive specificity in freshly explanted and cultured cells. J Cell Biol 90:55-62, 1981.

9. Sieber F, Stuart RK and Spivak JL: Tumor-promoting phorbol esters stimulate myelopoiesis and suppress erythropoiesis in cultures of mouse bone marrow cells. Proc Natl Acad Sci USA 78:4402-4406, 1981.

10. Sieber-Blum M and Sieber F: Tumor-promoting phorbol esters promote melanogenesis and prevent expression of the adrenergic phenotype in quail neural crest cells. Differentiation 20:117-123, 1981.

11. Kuhlenschmidt MS, Schmell E, Slife CW, Kuhlenschmidt TB, Sieber F, Lee, YC and Roseman S: Studies on the intercellular adhesion of rat and chicken hepatocytes: conditions affecting cell-cell specificity. J Biol Chem 257:3157-3164, 1982.

12. Sieber F and Sharkis SJ: Modulation of murine erythropoiesis in vitro by syngeneic thymocytes: interactions of enhancing and suppressing subpopulations with fluorescent anti-theta antibody and polyamino acids. Blood 60:845-849, 1982.

13. Meagher RC, Sieber F and Spivak JL: Suppression of hematopoietic progenitor cell proliferation by ethanol and acetaldehyde. N Engl J Med 307:845-849, 1982.

14. Dover GJ, Chan T and Sieber F: Fetal Hemoglobin production in cultures of primitive and mature human erythroid progenitors. Differentiation affects the quantity of fetal hemoglobin produced per cell not the number of fetal hemoglobin-containing cells. Blood 61:1242-1246, 1983.

15. Meagher RC, Sieber F and Spivak JL: Susceptibility to merocyanine 540-mediated photosensitization: a differentiation marker on murine hematopoietic progenitor cells. J Cell Physiol 116:118-124, 1983.

16. LaRussa VF, Sieber F, Sensenbrenner LL and Sharkis SJ: Effects of neuraminidase on the regulation of erythropoiesis. Blood 63:784-788, 1984.

17. Sieber-Blum M. and Sieber F.: Heterogeneity among early quail neural crest cells. Develop Brain Res 14:241-246, 1984.

18. Sieber F, Spivak JL and Sutcliffe AM: Selective killing of leukemic cells by merocyanine 540-mediated photosensitization. Proc Natl Acad Sci USA 81:7584-7587, 1984.

19. Sieber F and Sieber-Blum M: Dye-mediated photosensitization of murine neuroblastoma cells. Cancer Res 46:2072-2076, 1986.

20. Sieber F, Rao S, Rowley SD and Sieber-Blum M: Dye-mediated photolysis of human neuroblastoma cells: Implications for autologous bone marrow transplantation. Blood 68:32-36, 1986.

21. Levine RF, Spivak JL, Meagher RC and Sieber F: Effect of ethanol on thrombopoiesis. Br J Haematol 62:345-354, 1986.

22. Sieber F, Stuart RK, Rowley SD, Sharkis SJ and Sensenbrenner LL: Dye-mediated photolysis of normal and neoplastic hematopoietic cells. Leukemia Res 11:43-49, 1987.

23. Sieber F.: Elimination of residual tumor cells from autologous bone marrow grafts by dye-mediated photolysis: preclinical data. Photochem Photobiol 46:71-76, 1987.

24. Kalyanaraman B, Feix JB, Sieber F, Thomas JP and Girotti AW: Photodynamic action of merocyanine 540 on artificial and natural cell membranes: Involvement of singlet molecular oxygen. Proc Natl Acad Sci USA 84:2999-3003, 1987.

25. Sieber F, O'Brien JM, Krueger GJ, Schober SL, Burns WH, Sharkis SJ and Sensenbrenner LL: Antiviral activity of merocyanine 540. Photochem Photobiol 46:707-711, 1987.

26. Sieber F, Krueger GJ, O'Brien JM, Schober SL, Sensenbrenner LL and Sharkis SJ: Inactivation of Friend erythroleukemia virus and Friend virus-transformed cells by merocyanine 540-mediated photosensitization. Blood 73:345-350, 1989.

27. O'Brien JM and Sieber F: Mutagenicity of merocyanine 540-mediated photosensitization. Exp Hematol 17:166-170, 1989.

28. Sieber F and Krueger GJ: Photodynamic therapy and bone marrow transplantation. Sem Hematol 26:35-39, 1989.

29. Gaffney DK, Schober SL and Sieber F: Merocyanine 540-sensitized photoinactivation of leukemia cells: Role of oxygen and effects on plasma membrane integrity and mitochondrial respiration. Exp Hematol 18:23-26, 1990.

30. Smith OM and Sieber F: Antineoplastic and virucidal effects of merocyanine 540. Trends in Photochemistry & Photobiology 1:49-59, 1990.

31. O'Brien JM, Montgomery RR, Burns WH, Gaffney DK and Sieber F: Evaluation of merocyanine 540-sensitized photoirradiation as a means to inactivate enveloped viruses in blood products. J Lab Clin Med 116:439-447, 1990.

32. Gaffney DK and Sieber F: Merocyanine 540-sensitized photoinactivation of soluble and membrane-bound enzymes in L1210 leukemia cells. Cancer Res 50:7765-7769, 1990.

33. Gaffney DK, O'Brien JM and Sieber F: Modulation by thiols of the merocyanine 540-sensitized photolysis of leukemia cells, red cells, and herpes simplex virus type 1. Photochem Photobiol 53:85-92, 1991.

34. Smith OM, Traul DL, McOlash L and Sieber F: Evaluation of merocyanine 540-sensitized photoirradiation as a method for purging malarially-infected red cells from blood. J Infect Diseases 163:1312-1317, 1991.

35. Lum LG, Yamagami M, Giddings BR, Joshi I, Schober SL, Sensenbrenner LL and Sieber F: The immunoregulatory effects of merocyanine 540 on in vitro human T and B lymphocyte functions. Blood 77:2701-2706, 1991.

36. Smith OM, Gaffney DK, Anderson MS, McOlash L, Schober SL and Sieber F: Plasma membrane properties regulating the sensitivity of leukemia, lymphoma, and solid tumor cells to merocyanine 540-sensitized photoirradiation. Exp Hematol 19:785-788, 1991.

37. Gaffney DK, Feix JB, Schwarz HP, Struve MF and Sieber F: Cholesterol content but not plasma membrane fluidity influences the susceptibility of L1210 leukemia cells to merocyanine 540-sensitized irradiation. Photochem Photobiol 54:717-723, 1991.

38. O'Brien JM, Singh RJ, Feix JB, Kalyanaraman B and Sieber F: Action spectra of the antileukemic and antiviral activities of merocyanine 540. Photochem Photobiol 54:851-854, 1991.

39. Itoh T, Gaffney DK, and Sieber F: Merocyanine 540 as a marrow purging agent: Split addition of dye in two half-doses reduces toxicity to normal hematopoietic stem cells without reducing the antineoplastic effect. Cancer Ther Contr 2:251-258, 1992.

40. Whelan HT, Traul DL, Przybylski C, Segura A, Thomas J, Meyer G and Sieber F: Interactions of merocyanine 540 with human brain tumor cells. Ped Neurol 8:117-120, 1992.

41. Qiu K, Traul DL and Sieber F: Limited cell-cycle dependence of the merocyanine 540-sensitized photoinactivation of L1210 leukemia cells. Photochem Photobiol 56:277-280, 1992.

42. Qiu K and Sieber F: Merocyanine 540-sensitized photoinactivation of leukemia cells: Effects of dose fractionation. Photochem Photobiol 56:489-493, 1992.

43. O'Brien JM, Gaffney DK, Wang TP and Sieber F: Merocyanine 540-sensitized photoinactivation of enveloped viruses in blood products: Site and mechanism of phototoxicity. Blood 80:277-285, 1992.

44. Smith OM, Dolan SA, Dvorak JA, Wellems TE and Sieber F: Merocyanine 540-sensitized photoinactivation of human erythrocytes parasitized by Plasmodium falciparum. Blood 80:21-24, 1992.

45. Smith OM, Traul DL and Sieber F: Photodamaging effects of merocyanine 540 on neutrophils and HL-60 cells. Exp Hematol 20:1278-1284, 1992.

46. Gaffney DK and Sieber F: The role of serum and serum components in the merocyanine 540-sensitized photoinactivation of K562 leukemia cells. Biochim Biophys Acta 1117:321-325, 1992.

47. Smith OM, Qiu K, Witt PL, Borden EC and Sieber F: Merocyanine 540 and two-phase partitioning detect interferon-β_{ser}-induced plasma membrane alterations in Daudi lymphoma cells. Cancer Res Ther Contr 3:87-93, 1993.

48. Qiu K and Sieber F: Pharmacokinetics of merocyanine 540. Cancer Res Ther Contr 3:239-243, 1993.

49. Itoh T, Messner HA, Jamal N, Tweeddale M and Sieber F: Merocyanine 540-sensitized photoinactivation of high-grade non-Hodgkin's lymphoma cells: Potential application in autologous bone marrow transplantation. Bone Marrow Transpl 12:191-196, 1993.

50. Krieg M, Bilitz JM, Traul DL and Sieber F: Photosensitizing oxonol dyes with antineoplastic activity. Cancer Res Ther Contr 4:163-172, 1995.

51. Traul DL, Anderson GS, Bilitz JM, Krieg M and Sieber F: Potentiation of Merocyanine 540-mediated photodynamic therapy by salicylate and related drugs. Photochem Photobiol 62:790-199, 1995.

52. Anderson GS, Günther WHH, Searle R, Bilitz JM, Krieg M and Sieber F: Inactivation of photosensitizing merocyanine dyes by plasma, serum, and serum components. Photochem Photobiol 64:683-687, 1996.

53. Yamazaki T and Sieber F: The alkyl-lysophospholipid, ET-18-OCH_3 synergistically enhances the Merocyanine 540-mediated photoinactivation of leukemia cells: Implications for the extracorporeal purging of autologous hematopoietic stem cells. Bone Marrow Transpl 19:113-119, 1997.

54. Yamazaki T and Sieber F: Effect of hypothermia on the Merocyanine 540-mediated purging of hematopoietic cells. J Hematother 6:31-39, 1997.

55. Yamazaki T, Sato Y and Sieber F: Role of cytoprotective mechanisms in the photochemical purging of autologous bone marrow grafts. Exp Hematol 25:629-637, 1997.

56. Kubo Y and Sieber F: Photochemical purging of autologous bone marrow grafts: Assessment of damage to stem cells and the microenvironment in long-term marrow cultures. Bone Marrow Transpl 20:27-31, 1997.

57. Sato Y, Daziano J-P and Sieber F: Photochemical purging of autologous stem cell grafts: Potentiation of the antileukemic activity of Merocyanine 540 by ethacrynic acid. Cancer Res Ther Contr 5:241-251, 1998.

58. Indig GL, Anderson GS, Nichols MG, Barlett JA, Mellon WS and Sieber F: Effect of molecular structure on the performance of triarylmethane dyes as therapeutic agents for photochemical purging of autologous bone marrow grafts from residual tumor cells. J Pharm Sci 89:88-99, 2000.

59. Tsujino I and Sieber F: Genetic variability in the response of normal murine hematopoietic progenitor cells to extracorporeal photochemotherapy. Photochem Photobiol 72:810-814, 2000.

60. Tsujino I, Anderson GS and Sieber F: Post-irradiation hyperthermia selectively potentiates the Merocyanine 540-sensitized photoinactivation of small cell lung cancer cells. Photochem Photobiol 73:191-198, 2001.

61. Anderson GS, Miyagi K, Sampson RW and Sieber F: Anti-tumor effect of Merocyanine 540-mediated photochemotherapy combined with Edelfosine: Potential implications for the ex vivo purging of hematopoietic stem cell grafts from breast cancer patients. J Photochem Photobiol B: Biology 68:101-108, 2002.

62. Anderson GS, Tsujino I, Miyagi K, Sampson RW and Sieber F: Preferential inactivation of paediatric solid tumour cells by sequential exposure to Merocyanine 540-mediated photodynamic therapy and Edelfosine: Implications for the ex vivo purging of autologous haematopoietic stem cell grafts. J Photochem Photobiol B: Biology 69:87-95, 2003.

63. Miyagi K, Sampson RW, Sieber-Blum M and Sieber F: Crystal violet and Merocyanine 540 for the ex vivo purging of hematopoietic stem cell grafts. J Photochem Photobiol B: Biology 70:133-144, 2003.

64. Tsujino I, Miyagi K, Sampson RW and Sieber F: Potentiation of the anti-tumor effect of Merocyanine 540-mediated photodynamic therapy by amifostine and amphotericin B. Photochem Photobiol, 82:458-465, 2006.

CHAPTERS AND REVIEWS

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